Article 7 - Replication of a synthetic oligomer using chameleon base-pairs

Núñez-Villanueva, D.; Hunter, C. A. Replication of a Synthetic Oligomer Using Chameleon Base-Pairs. Chemical Communications 2022, 58 (78), 11005–11008. https://doi.org/10.1039/d2cc04580j.

Figure 1:

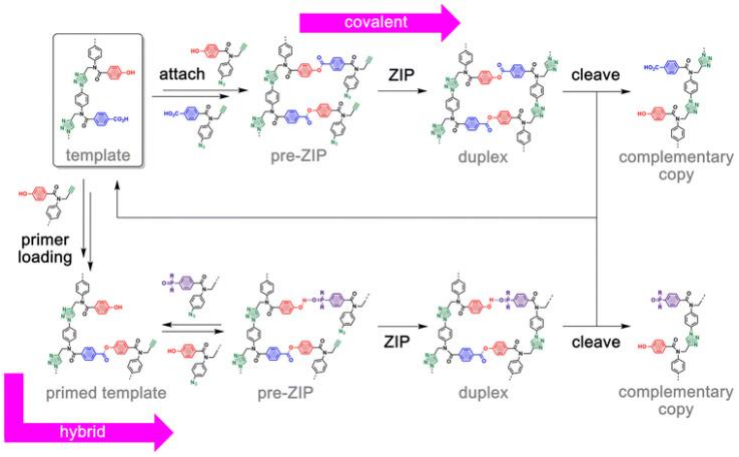

Figure 1 illustrates two strategies for replicating triazole oligomers: fully covalent replication and a hybrid covalent/non-covalent method. In the fully covalent method, phenol and benzoic acid monomers are attached to the template by ester coupling, followed by a CuAAC reaction that forms a covalent duplex. The template is then cleaved to release both the template and its complementary copy. In the hybrid method, a covalent primer is loaded onto the template, and non-covalent hydrogen bonding between phenol and phosphine oxide units helps form a pre-ZIP complex. This complex undergoes a CuAAC reaction to extend the primer, and hydrolysis of the ester bond releases the complementary copy. The hybrid method allows for efficient replication with short primers, mimicking aspects of natural replication processes.

Synopsis:

The replication of genetic information is a cornerstone of natural biology, with nucleotide base-pairing serving as the foundation for accurate information transfer. In synthetic systems, mimicking this process has posed significant challenges, inspiring researchers to develop artificial base-pairing systems known as unnatural base pairs. These systems aim to expand the genetic code and create new molecular architectures. The article "Replication of a Synthetic Oligomer Using Chameleon Base-Pairs," by Diego Núñez-Villanueva and Christopher A. Hunter, presents an innovative solution: a dynamic approach leveraging chameleon base-pairs to replicate synthetic oligomers with high fidelity.

Chameleon base pairs are designed to switch their recognition properties under specific conditions, enabling the assembly and disassembly of synthetic oligomers. This adaptability is

key to the study’s success. The researchers focus on a system where benzoic acid recognition units on a template oligomer interact with amidine monomers through salt bridge formation. This interaction acts as a guide, facilitating the assembly of a complementary oligomer and effectively replicating the original template.

The replication process involves several critical steps. First, the benzoic acid 3-mer template interacts with amidine monomers, forming a pre-zip intermediate through salt bridges. This assembly is then polymerized along the template using a copper-catalyzed azide-alkyne cycloaddition reaction, resulting in a non-covalent duplex. Finally, ester linkers are hydrolyzed, removing the amidine recognition units and converting them into benzoic acid units. This crucial step regenerates the original template and releases a replicated benzoic acid 3-mer, completing the replication cycle.

The study’s findings underscore the effectiveness of the chameleon base-pair system. Templated oligomerization consistently produces the amidine 3-mer copy as the major product, showcasing the method's high fidelity. The cleavage of ester linkers ensures the replicated oligomer mirrors the original template’s structure, confirming the system’s reliability. This innovative approach demonstrates the potential of chameleon base pairs to expand the genetic alphabet and create complex molecular architectures.

A key figure in the article encapsulates the entire replication process. It depicts the pre-zip intermediate formed by the template and amidine monomers, the polymerization step creating the non-covalent duplex, and the cleavage step releasing the replicated oligomer. This visual representation highlights the system's elegance and efficiency, emphasizing the chameleon base-pairs dynamic nature in facilitating replication.

The research by Núñez-Villanueva and Hunter marks a significant advancement in supramolecular chemistry. By leveraging the adaptability of chameleon base pairs, this study achieves synthetic oligomer replication and opens doors to new possibilities in molecular replication and synthetic polymer design. The approach demonstrates a promising future for creating programmable molecular systems with unprecedented capabilities.